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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/535,345	02/15/2006	Graeme Semple	22578-005US1 079.US2.PCT	6159

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EXAMINER	
CHUNG, SUSANNAH LEE	
ART UNIT	**PAPER NUMBER**
1626	
MAIL DATE	**DELIVERY MODE**
06/24/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/535,345	SEMPLE ET AL.	
	Examiner	Art Unit	
	SUSANNAH CHUNG	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4,7,10,11,14,17-22,26-31 and 41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4,7,10,11,14,17-22,26-31 and 41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/5/06, 1/15/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 4, 7, 10-11, 14, 17-22, 26-31, and 41 are pending in the instant application. Claims 1-3, 5-6, 8-9, 12-13, 15-16, 23-25, 32-40, and 42 are canceled by preliminary amendment.

Priority

This application is a 371 of PCT/US04/35927, filed 10/29/2004, which claims benefit of 60/516,238, filed 10/31/2003.

Information Disclosure Statement

The information disclosure statement (IDS), filed on 4/5/06 and 1/15/08 have been considered. Please refer to Applicant's copy of the 1449 submitted herewith.

Response to Election/Restrictions

Applicant's election with traverse of Group I in the reply filed on 5/19/08 is acknowledged.

The traversal is on the following grounds that the basis of the restriction was not for a 371 application, but rather a US application and thus rejoinder is requested. **The restriction requirement mailed on 1/17/2008 is withdrawn** and all the claims are examined for patentability.

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 28-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not enable one skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims, for the reasons describe below.

As stated in MPEP 2164.01(a), "there are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue."

The factors to be considered when determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, were described in In re Wands, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) as:

1. the nature of the invention;
2. the breadth of the claims;
3. the state of the prior art;
4. the relative skill of those in the art;
5. the predictability or unpredictability of the art;
6. the amount of direction or guidance presented [by the inventor];
7. the presence or absence of working examples; and
8. the quantity of experimentation necessary [to make and/or use the invention].

The eight Wands factors are applied to Claims 28-31 of the present invention below:

(1) The Nature of the Invention

Claims 28-31 are directed to methods of treating a metabolic-related disorder and raising HDL comprising administering to an individual in need of such treatment a therapeutically effective amount of a compound of claim 4.

(2) The Breadth of the claims

Claims 28-31 will be give its broadest reasonable interpretation. The applicable rule for interpreting the claims is that "each claim must be separately analyzed and given its broadest reasonable interpretation in light of and consistent with the written description." See MPEP 2163(II)(1), citing In re Morris, 127 F.3d 1048, 1053-1054; 44 USPQ2d 1023, 1027 (Fed. Cir. 1997). In view of this rule, Claims 28 and 31, which do not specify the many possible metabolic-related disorders will be interpreted to encompass all metabolic-related disorders. Claims 29 and 30, which specify the disorders dyslipidemia, atherosclerosis, coronary heart disease, insulin resistance, and type 2 diabetes will be examined to see if there is support in the specification and prior art for these disorders, regardless of whether it is a primary or secondary method of use.

(3) The state of the prior art

The state of the art at the time of this application was that certain benzotriazole compounds exhibit useful pharmaceutical properties as PPAR agonists and could be used to treat dyslipidemic type 2 diabetes or dyslipidemia without diabetes. (See Sparatore, et al., Chem & Biodiver., Vol. 3, 2006, 385-395, especially page 390, approx. lines 10-15.)

The use of benzotriazole compounds as selective agonists of the Human Orphan G-Protein-Coupled Receptor GPR109b is also known. Studies have shown that the benzotriazole

derivatives can be used to treat dyslipidemia and atherosclerosis. (See Semple, et al., J. Med. Chem. 2006, 49, 1227-1230, especially page 1229, column 2, approx. lines 28-31.)

It should be noted that the instant application is not directed to benzotriazole agonists of PPAR or GPR109b, but rather tetrazole agonists of RUP25. The, current state of the art is that benzotriazole compounds are useful in treating some diseases wherein the mechanism of action is PPAR or GPR109b, but the utility of tetrazole compounds as RUP25 agonists is not well known. Therefore, guidance is sought from the instant specification as to whether these compounds are enabled as RUP25 agonists and could treat specific disorders.

(4) The relative skill of those in the art

The level of skill in the art (pharmaceutical chemists, physicians) would be high.

(5) The predictability or unpredictability of the art

It is noted that the pharmaceutical art generally is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement varies inversely with the degree of unpredictability in the factors involved. In re Fisher, 427 F.2d 833, 839. Therefore, the more unpredictable an area, the more specific enablement is needed in order to satisfy the statute. Added to the unpredictability of the art itself is the question whether the compound of the present invention could be reliably and predictably extrapolated to patients with all the metabolic-related disorders claimed. There is no absolute predictability, even in view of the high level of skill in the art.

(6) The amount of direction or guidance presented (by the inventor)

The specification in the present invention discloses that the instantly claimed compounds can be used to treat metabolic-related disorders. The mechanism of action used by the instantly claimed tetrazole compounds is that they are agonists of RUP25. Applicants provide some data, but do not show with any level of specificity how the instantly claimed compounds are agonists of RUP25 or how they treat specific metabolic-related disorders. Therefore, there is insufficient guidance in the specification for the role the instantly claimed compounds play as agonists of RUP25 or the role the instantly claimed compounds play in treating all metabolic related disorders, including, but not limited to dyslipidemia, atherosclerosis, coronary hear disease, insulin resistance, and type 2 diabetes.

(7) The presence or absence of working examples

The specification discloses the general role of the instantly claimed tetrazole compounds as RUP25 agonists on pages 32-34 of the specification, but the data provided does not show how the instantly claimed compounds are RUP25 agonists or how the instantly claimed compounds act to treat a disorder. In particular, there are no working examples of how a particular compound is used to treat a particular disorder or of the general mechanism of action used as an RUP25 agonist. Simply stating that a compound can treat a disorder is not sufficient. Specific data should be provided showing the results of the tests.

In addition, Applicants state that in vitro and in vivo tests were performed on page 45 of the specification. On page 48-59 of the specification, animal model and binding assay data are provided, but the animal models and assays do not provide specific data showing the binding capability of any of the instantly claimed compounds.

(8) The quantity of experimentation necessary (to make and/or use the invention)

Given the absence of direction or guidance (or working examples) in the specification for the role of the instantly compounds as RUP25 agonists to treat metabolic disorders or raise HDL levels in general, it would cause a skilled artisan an undue amount of experimentation to practice this invention to determine which patients with which diseases would benefit from which of the many claimed compounds within the scope of the invention with a reasonable expectation of success. Therefore, the claims are not enabled.

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4, 7, 10, 11, 14, 17-22, 26-28, 31 and 41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compounds and compositions of claim 4, does not reasonably provide enablement for solvates or hydrates of those compounds. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The claims recite specific compounds, the solvates and hydrates of said compounds. However, the specification fails to teach the preparation of solvates or hydrates. Therefore, the specification is not adequately enabled for solvates and hydrates.

Identifying a solvate requires knowledge of properties of the solvents and solutes of the instant compounds and nothing short of extensive testing (none identified) would be needed to determine if additional derivatives exist thus, such a scope as literally claimed herein is not enabled.

The examples presented all fail to produce a solvate or hydrate. These cannot be simply willed into existence. As was stated in Morton International Inc. v. Cardinal Chemical Co., 28 USPQ 2d 1190, "the specification purports to teach, with over fifty examples, the preparation of the claimed compounds with the required connectivity. However…there is no evidence that such compounds exist…the examples of the `881 patent do not produce the postulated compounds…there is…no evidence that such compounds even exist." The same circumstance appears to be true here. There is no evidence that solvates or hydrates of the instantly claimed compounds exist. If they did, they would have been formed. Hence, applications must show that solvates and hydrates can be made, or limit the claims accordingly by deleting the terms solvates and hydrates.

It is not the norm that one can predict with any accuracy a particular solvate form of an active compound will be more soluble, more easily handled in formulations or more bioavailable without actual testing in vivo. The specification provides no guidance as to what types are suitable for the instantly claimed compounds.

The factors to be considered when determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, were described in In re Wands, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) as:

1. the nature of the invention;
2. the breadth of the claims;
3. the state of the prior art;
4. the relative skill of those in the art;
5. the predictability or unpredictability of the art;

6. the amount of direction or guidance presented (by the inventor);

7. the presence or absence of working examples; and

8. the quantity of experimentation necessary (to make and/or use the invention).

The eight Wands factors are applied to Claims 4, 7, 10, 11, 14, 17-22, 26-28, 31 and 41 of the present invention below:

(1) The Nature of the Invention

The nature of the invention is the compounds of claim 4. In addition to the compounds, the salts, solvates and hydrates are also claimed.

(2) The Breadth of the claims

The breadth of the claims encompass salts, solvates and hydrates of the compounds of claim 4. The applicable rule for interpreting the claims is that "each claim must be separately analyzed and given its broadest reasonable interpretation in light of and consistent with the written description." See MPEP 2163(II)(1), citing In re Morris, 127 F.3d 1048, 1053-1054; 44 USPQ2d 1023, 1027 (Fed. Cir. 1997). In view of this rule, all of the potential salts, solvates and hydrates that could be formed will be interpreted to be encompassed by the instant claims.

(3) The state of the prior art

It was known in the art at the time of this application that compounds can exist in salt, solvate and hydrate form.

(4) The relative skill of those in the art

The level of skill in the art (pharmaceutical chemists, physicians) would be high.

(5) The predictability or unpredictability of the art

The predictability of the art with regard to salts is known, but the preparation of solvates and hydrates are compound specific. In addition, the extremely large scope of the potential solvates and hydrates that could be produced using the compounds of claim 4 renders the prior art unpredictable for making or using products as claimed on such a grand scale.

(6) The amount of direction or guidance presented (by the inventor)

There is no guidance in the specification drawn to the solvates and hydrates of the instantly claimed compounds. In addition, the specification provides no guidance as to what type(s) of solvates are suitable for the instantly claimed compounds.

(7) The presence or absence of working examples

The specification has no working examples of solvates or hydrates of the instantly claimed compounds.

(8) The quantity of experimentation necessary (to make and/or use the invention)

The quantity of experimentation is undue given the absence of direction or guidance (or working examples) in the specification for the extremely large number of solvates and hydrates that could be encompassed by the claims. Identifying a solvate requires knowledge of the properties of the solvents and solutes and their reactions and/or transformation, nothing short of extensive testing (none identified) would be needed to determine if additional derivatives exist and thus, such as scope as literally claimed herein is non-enabled.

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 41 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the claim is indefinite and incomplete for omitting essential process steps, such omission amounting to a gap between the steps. See MPEP §2172.01. The omitted steps are the reagents used and specific steps of preparing the composition of claim 4. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Obviousness Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 28-31 and 41 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 28-31 and 41-43 of copending application number 11/601,252.

This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

Applicants instant elected invention discloses methods of treatment using the compounds of claim 4, wherein the disorder is a metabolic disorder, such as dyslipidemia, atherosclerosis, coronary heart disease, insulin resistance, and type 2 diabetes.

Co-pending application No. 11/601,252 claims methods of treatment using the compound of formula (Ih), wherein the disorder is a metabolic disorder, such as dyslipidemia, atherosclerosis, coronary heart disease, insulin resistance, and type 2 diabetes.

The difference between co-pending application and the instant application is that in the co-pending application is drawn to a larger class of compounds than the instant application.

One of ordinary skill in the art would have found the claimed methods prima facie obvious over the co-pending application because the methods of use are the same. Although the class of compounds in the instant application is more narrow than the copending application, the instantly claimed compounds fall within the preferred species of the copending application and one of ordinary skill in the art would use the teachings to discover the current utility. The motivation to claim the current utility is the expectation that structurally similar compounds would possess similar activity (i.e. pharmacological use in treating metabolic disorders). Although, the conflicting claims are not identical, they are not patentably distinct from each other because applicant's instantly claimed invention is disclosed in the co-pending application.

Therefore, one skilled in the art would have found the difference in scope obvious when faced with the co-pending applications because the compounds are used for the same pharmacological use so one skilled in the art would expect similar properties and results.

It is noted that the instant application is senior to the copending application and the rejection will be withdrawn should the case be found allowable.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susannah Chung whose telephone number is (571) 272-6098. The examiner can normally be reached on M-F, 8am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/REI-TSANG SHIAO /
Primary Examiner, Art Unit 1626

Susannah Chung, June 19, 2008